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Docket No.: 02567/100F496-US2
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Andrew Eisen

Application No.: 10/031,893

Confirmation Number: 8212

Filed: July 19, 2002

Art Unit: 1652

For: DROSOPHILA RECOMBINATION-
ASSOCIATED PROTEIN AND METHODS
FOR USE

Examiner: Richard G. HUTSON

SUBMISSION OF FORMAL DRAWINGS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Submitted herewith is one set (twenty-five sheets, figures 1A, 1B, 2A, 2B, 2C, 2D, 2E, 3A, 3B, 3C, 3D, 3E, 3F, 4A, 4B, 4C, 4D, 5A, 5B, 6A, 11, 6B, 6C, 6D, 6E, 6F, 7, 8, 9, 10, 12A, 12B, 13A and 13B) of formal drawings for filing in the above-identified patent application. Kindly substitute the enclosed formal drawings for the informal drawings currently present in the application.

Respectfully submitted,

Dated: December 12, 2003



Mitchell Bernstein, Ph.D.

Reg. No. 46,550

Agent for Applicant(s)

DARBY & DARBY P.C.
Post Office Box 5257
New York, NY 10150-5257
212-527-7700

FIG. 1A

DRAP Complete cDNA Clone Insert

agcgattacg gtagagatat ggtaatgcaa cgggtggatgt gaactccttg 50
gtttgcggtg aatgcgttca acggtggatc ttcgcttgca cctttcgcga 100
tagacgacat acggatacag atacagatac agaattggcct ccaacaacag 150
tagtaccacc gatctggaca gccagggtcaa tgtggaggat ttgcccataa 200
cgttcaagggt gaagtacatt ggttcggaag tggcacgtgg ctatggggc 250
attaagtata cgcgtcgtcc ggttgacata atggtgggcg tggccaaagaa 300
cctgcccgcc aataagggtgc tgcccgaactg cgaactgaag gtgtccaccg 350
acggagttcca gctggagatc atatcgccaa aggccagcat caatcactgg 400
agctatccca tcqacacgat ctcgatatggc gttcaggacc tggcttacac 450
aagggtcttt gccatgatcg tgggtgaagga cgaqtcqagt ccgcattccct 500
ttgagggttca cgccttcgtg tgcgacagtc gtgcgatggc gcggalagtg 550
acctttgccc tggccggccg ccttccagga ttactcgcga cgggtcaagg 600
aggcaaccgg tgaggaggag ggcgaggcca cggccagcga cactattaca 650
cccacgcgac acaagttcgc catcgatctg cgaacgccgg agaaattccag 700
gctggcgaaac tggagcagga aacggaggcg tagttatcct ggtgatccctg 750
cgttggctcc gtcaatgaga tgtgatgtgt tagttactta acgtccagtg 800

A ————— A

FIG. 1B

A ———— A

ttcactgtat	ctgtaaatg	tggttctctc	acctggtagt	tgcctcatac	850
agctaatat	ccaaagccta	agtgttaata	cgatttgtaa	acgatttcta	900
aaataaata	cgaatatggt	atgtttggct	atttgaattg	ggctacaacc	950
tgttgatatg	ccacttggca	aaaaaaaaa	acgccagcac	caattctttt	1000
acttctgttt	cttgtgaccg	acataaaaaga	tgcaccaaag	ctgctattcc	1050
accagcgttc	tttattccac	gcttgttttc	atcattttgt	cttcggttaag	1100
ataaattacg	taaagcacca	caggcatttt	tatgtatttc	tggagaatca	1150
taagatagca	gtcgaactaa	tgggtggtata	cctcccagag	atcttgtacg	1200
ttgcttggtt	ggatcatcca	tgtagcacaa	atgctgtaga	taggctgctg	1250
cattagcttt	tatagcacta	ctcggggttg	ttaaaaagct	tattactttct	1300
gaaagatttg	gatcccgcca	tctcattgta	gaacaaatat	cattttctga	1350
tccttcaatg	taatcatcct	tttcttcc			1378

Longest ORF

nt 104 - 610

Probable Start Codon

nt 134

CDS Expressed as Recombinant Protein

nt 134 - 610

DRAP Coding Sequence - Restriction Map

MaxCuts: 1

B a e H
C j e H
M m e H
D r d H

193

1

P S Q I 4 0 6 H

B S at A I

att

A

A

gggtattgcaagtccacttcattcatgtaaccaaggcttcacggtgacccaataccccgtaa

৯

1

T

ttcatatgccagcaggccaaactgtattaccaccgcaccggttcttggacggcggggtta

9

4

88

8

— — — — —

373

1

I

38

५२

 \mathbb{R}^2

II

-

433

1

○

FIG. 2D

—

b b S P K A S I N H W S Y P I D T I S Y G V -

5
[w]

၈၆

esop

A0sAa58

v1plue6

a05w9x4

I9IN6A7

IIII

///

caggacctggtctacacaagggctcttgccatgatcgtggtgaaggacgagtcgagtcgcg
434 -----+-----+-----+-----+-----+-----+-----+
493

gtcctggaccagatgtgtccagaaacggtagcaccacttctgtgctcagctcagc

Q D L V Y T R V F A M I V V K D E S S P -

B
H

U
H

४
५

I

catcccttgagggttcacgccttcgtgtgcgacagtcgtgcgatggcgcggaagttagacc

-----D-----D-----

FIG. 2E

— — — — — D

494 -----+-----+-----+-----+-----+-----+-----+-----
gtaggaaactccaagtgcggaagcacacgctgtcagcacgcta|ccggcgcttcaactgg

b b H P F E V H A F V C D S R A M A R K L T -

B s a J I I
 N g O E F s I g e E I I
 B
 N r u I
 B s c G I I
 P i n A I I

tttgccctggcgcgccttccaggattactcgacggtcaaggaggaaccggtga
-----+-----+-----+-----+-----+-----613

aacgggaccgccggcggaaggtcctaataatgagcgctgccagttcctccgttgccact

b F A L A G R L P G L L A T G Q G G N R * -

ggaggag
614 -----+ 620
cctctc

1 6 6 4

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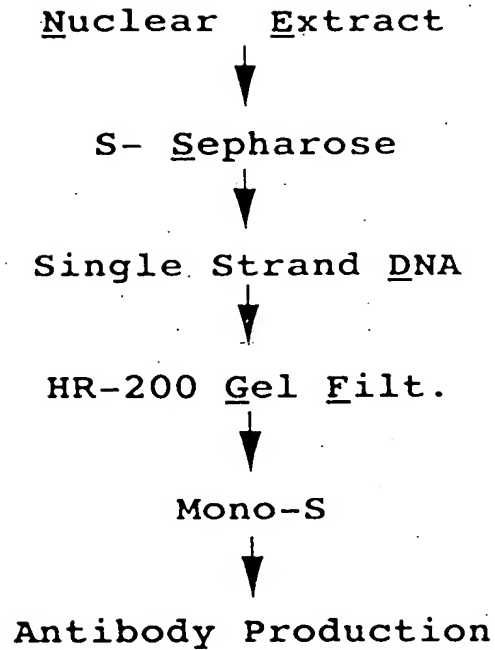
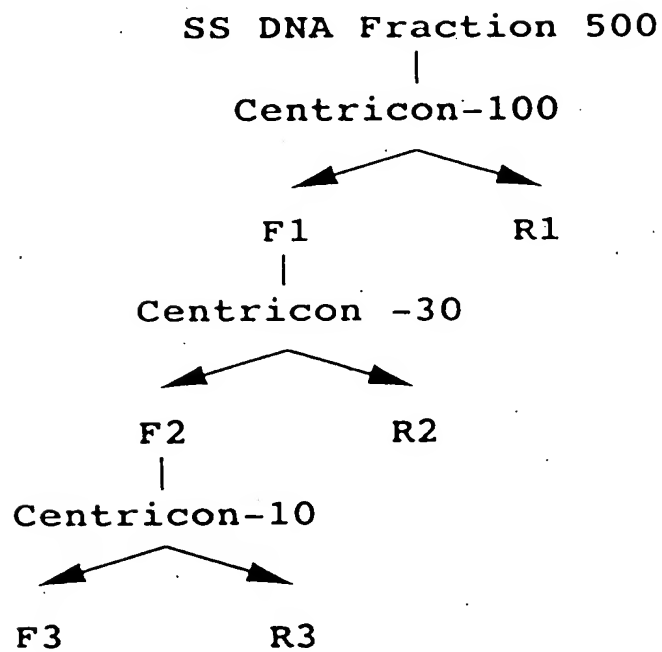


FIG. 3A

FIG. 3B



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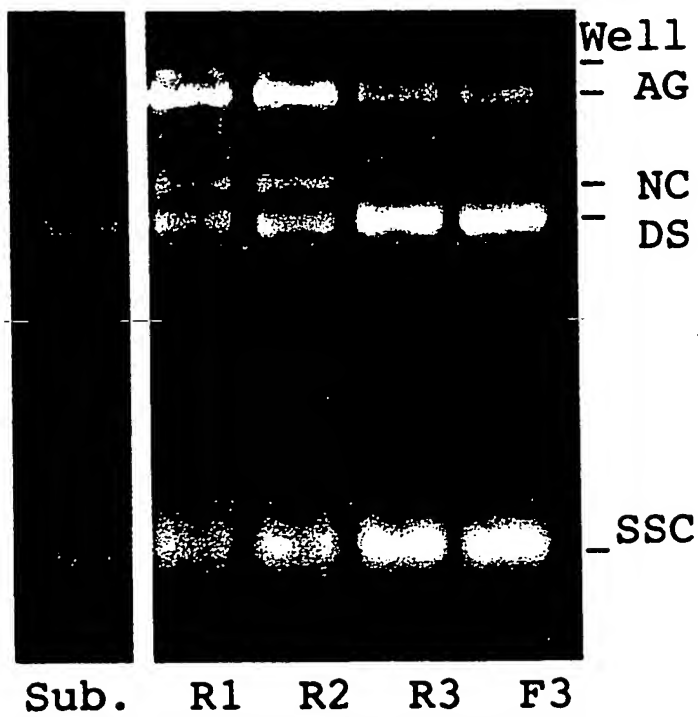
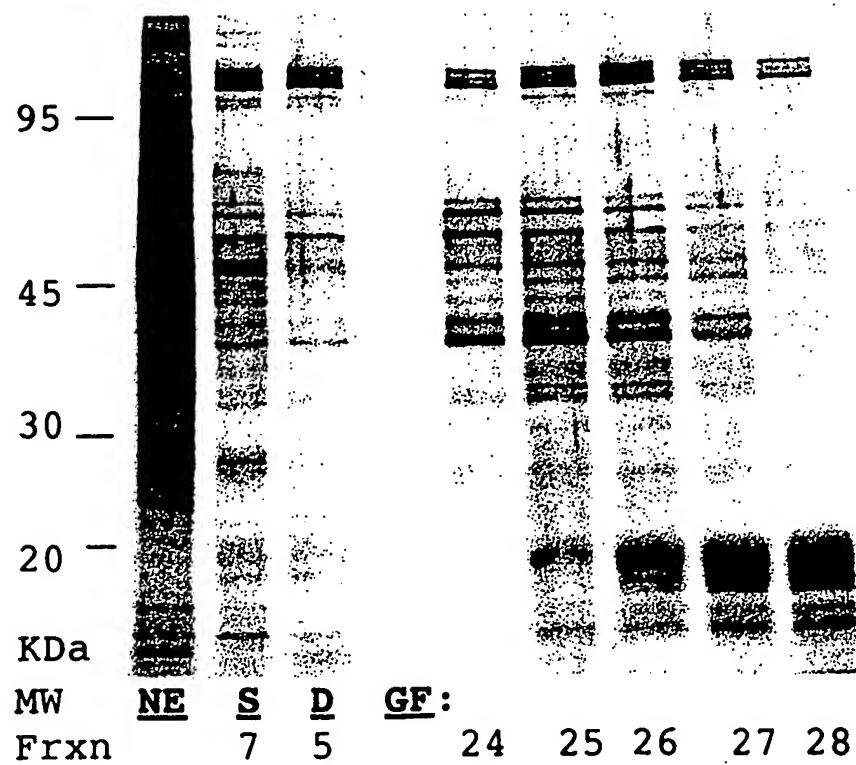


FIG. 3C

FIG. 3D



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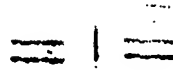


FIG. 3E



GF:

#28	#28
674	A-7
PAb	MAb



— 95



— 45

— 30



— 20

KDa

A7--Eluate

FIG. 3F

FIG. 4A

DRAP: 1378 bp Eco RI insert
ORF 104-610

1	134	281	902	970	1378
	ATG	ATG	AATAAA	(A)12	(A)29
	#1	#50			



FIG. 4B

→	MASNNSSSTD	LDSQVNVEDL	PITFKVKYIG	SEVARGLWGI	KYTRRPVDIM	50
..					2	
	VGVAKNLPPN	KVLPNCELKV	STDGVQLEII	SPKASINHWS	YPIDTISYGV	100
	QDLVYTRVFA	MIVVKDESSP	HPFEVHAFVC	DSRAMARKLT	FALACRLPGL	150
		1		3		
	LATGQGGNR					159

FIG. 4C

Potential	D1-----D2-----E1	Motifs
AA#s	(10 or 12)---(36 to 38)---(35+)---78	
	(19)---(54)---(44)---117	
	(19 or 48)---(46 to 75)---(30)---124	

FIG. 4D

Rad 51	Mouse - Human	L L I V - D - S
Rad 51	Yeast	L I V V - D - S
DCM 1	Yeast	L I V V - D - S
RecA	E. Coli	V I V V - D - S
Drosophila DRAP		M I V V K D E S S P
FLP Recombinase		M I A L K D E T N P
T4 Gene 32 Protein		I L V V K D P A A P
		M I A V - D V E M G E
		K - GFS S E
Human Topoisomerase I		I K D E - - P
		K D G S S E
		GFS S P

FIG. 5A

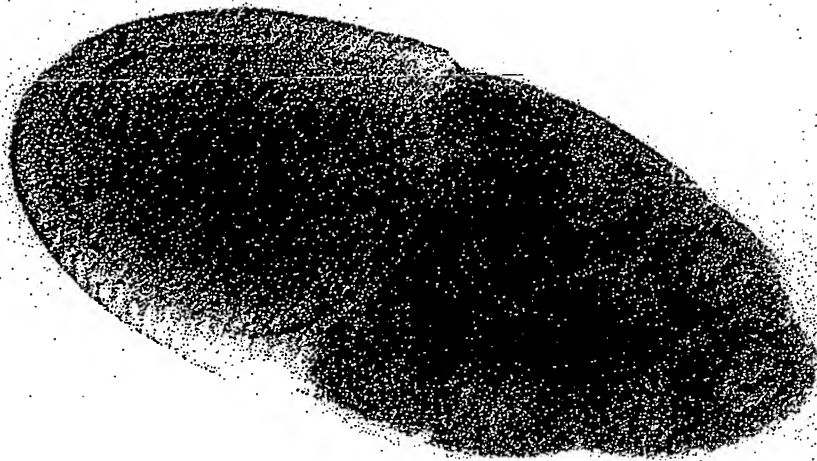


FIG. 5B

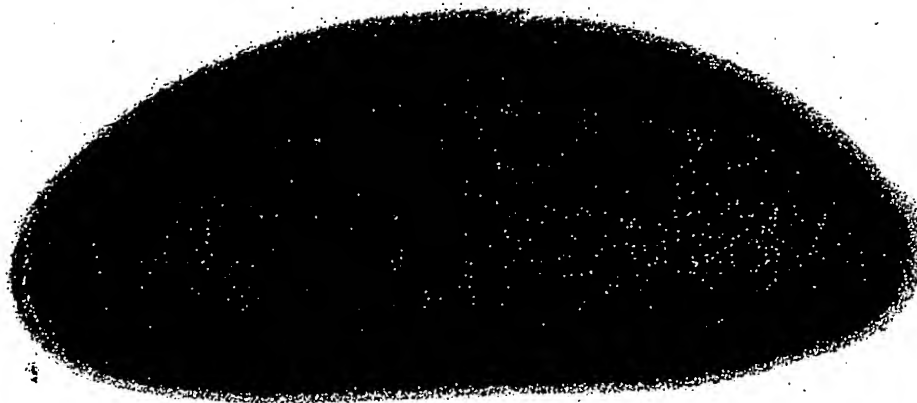
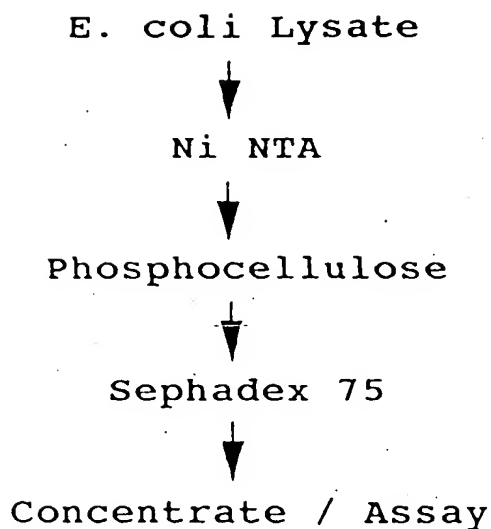


FIG. 6A**FIG. 11****Targeted Transgenics**

Gene	Oligo (No Phenotype)	Oligo + DRAP (Molar Ratio - Protein : Oligo)	
1. N - myc (Exon 1)	16	Low (1:1) High (100:1)	60 OK 4 Alive 11 Stillborn
2. β 1 globin (Ala --> Val)	7	High (100:1)	10 OK 5 Runts 4 OK 1 Sickly
3. Agouti	11	High (100:1)	8 OK

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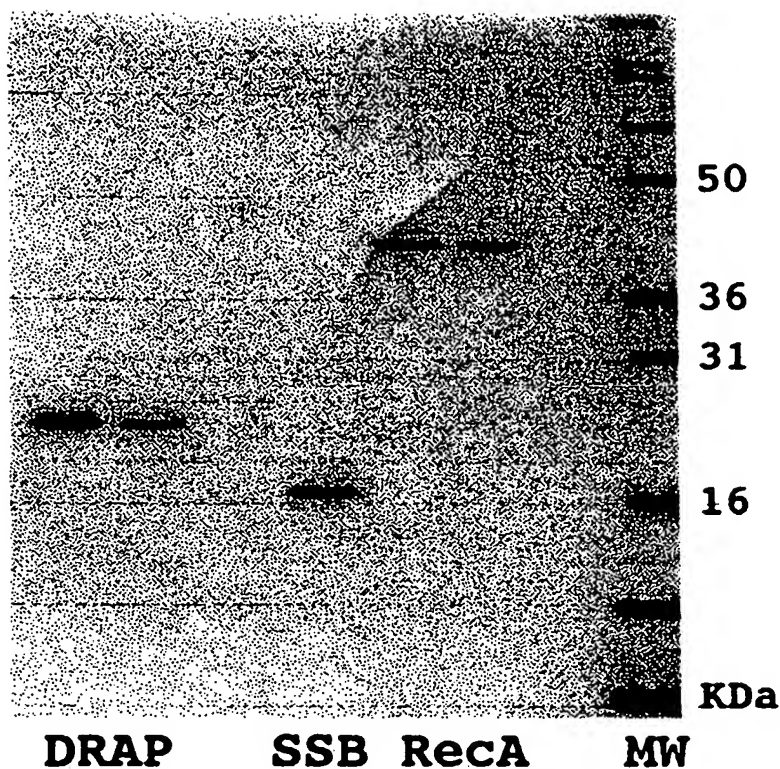


FIG. 6B

FIG. 6C

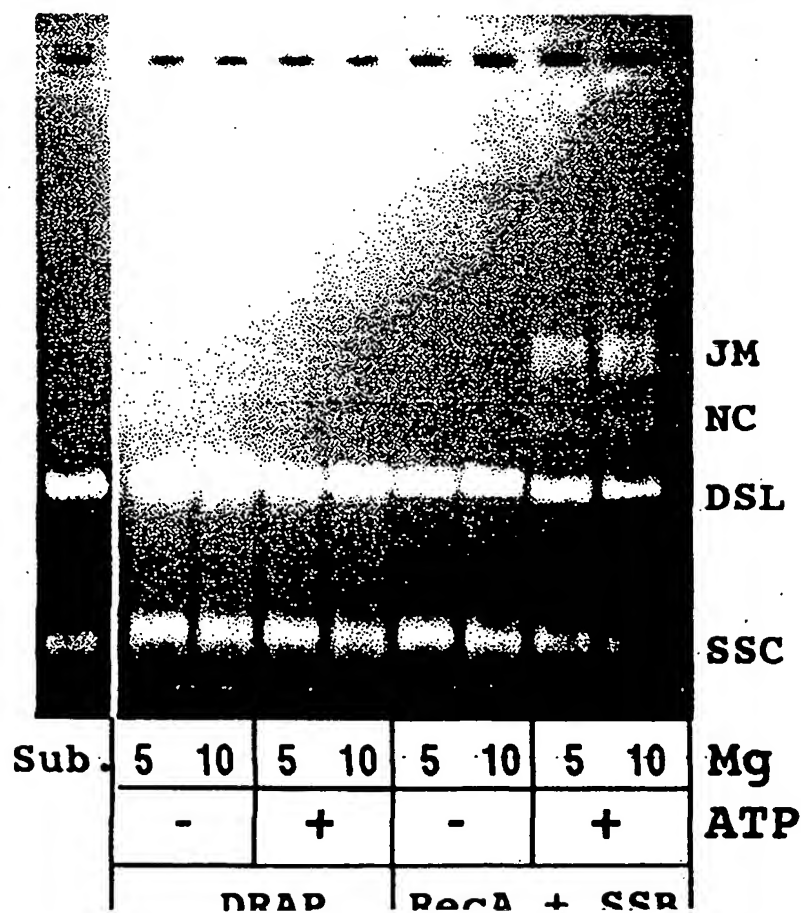


FIG. 6D

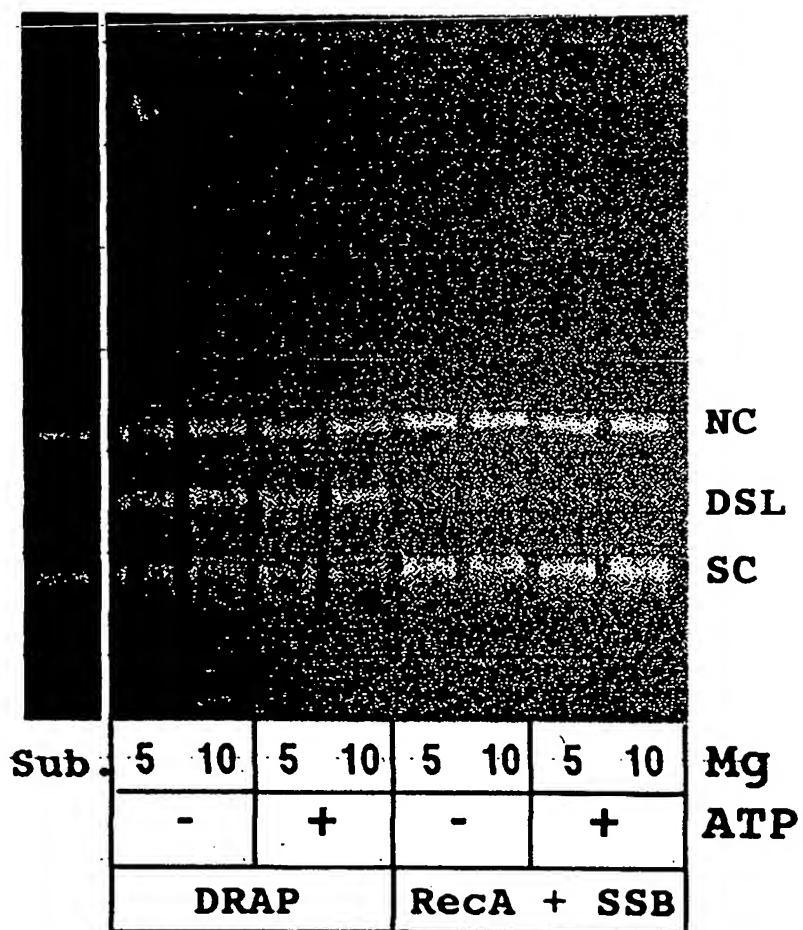


FIG. 6E

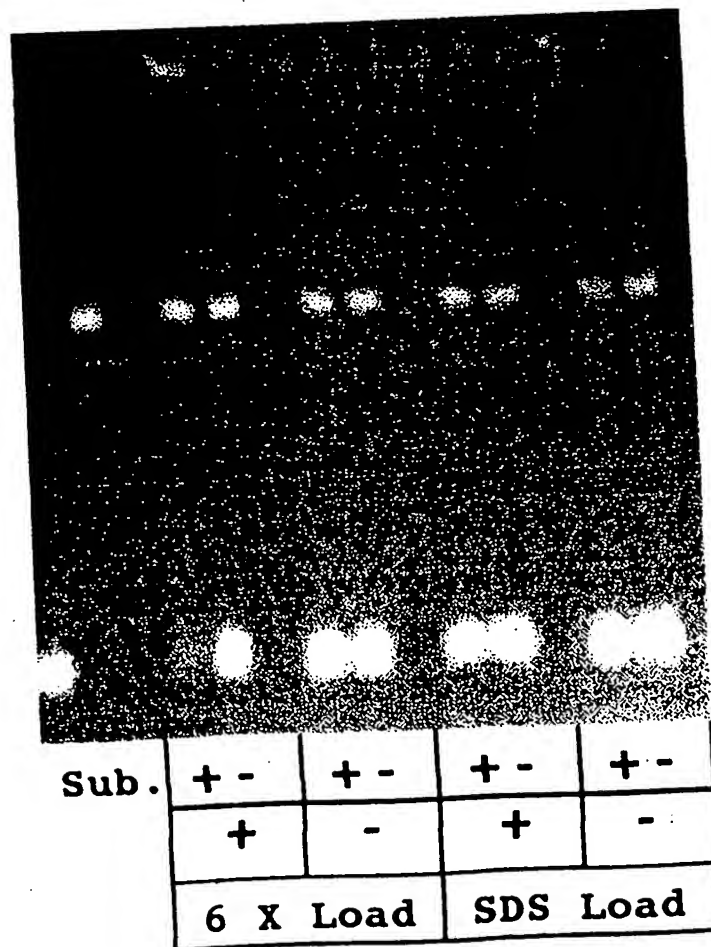
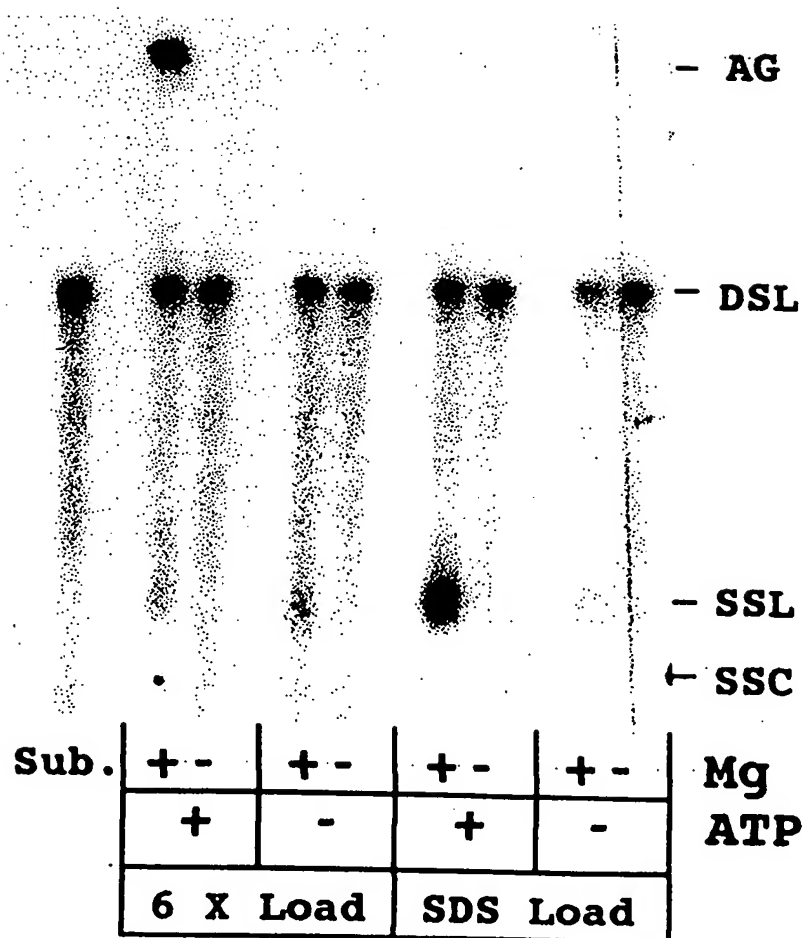


FIG. 6F



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FIG. 7

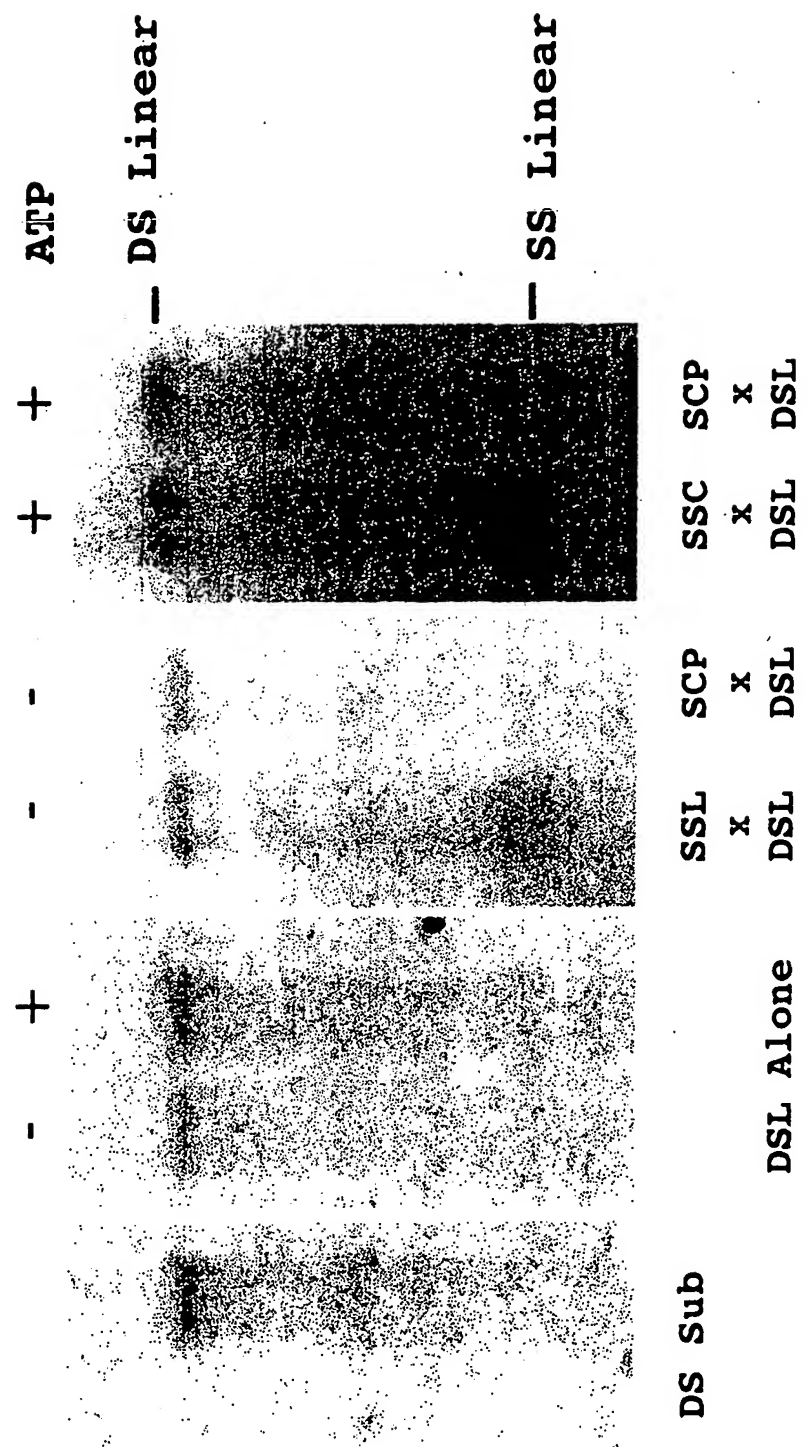
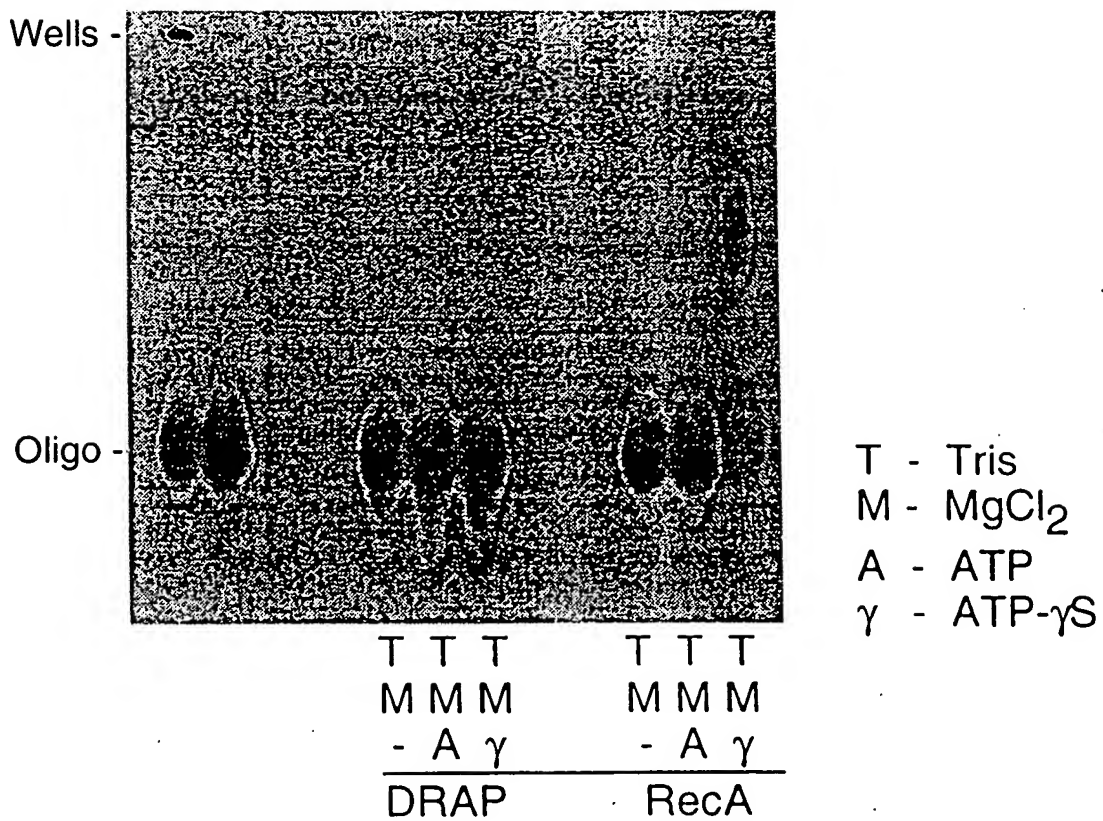
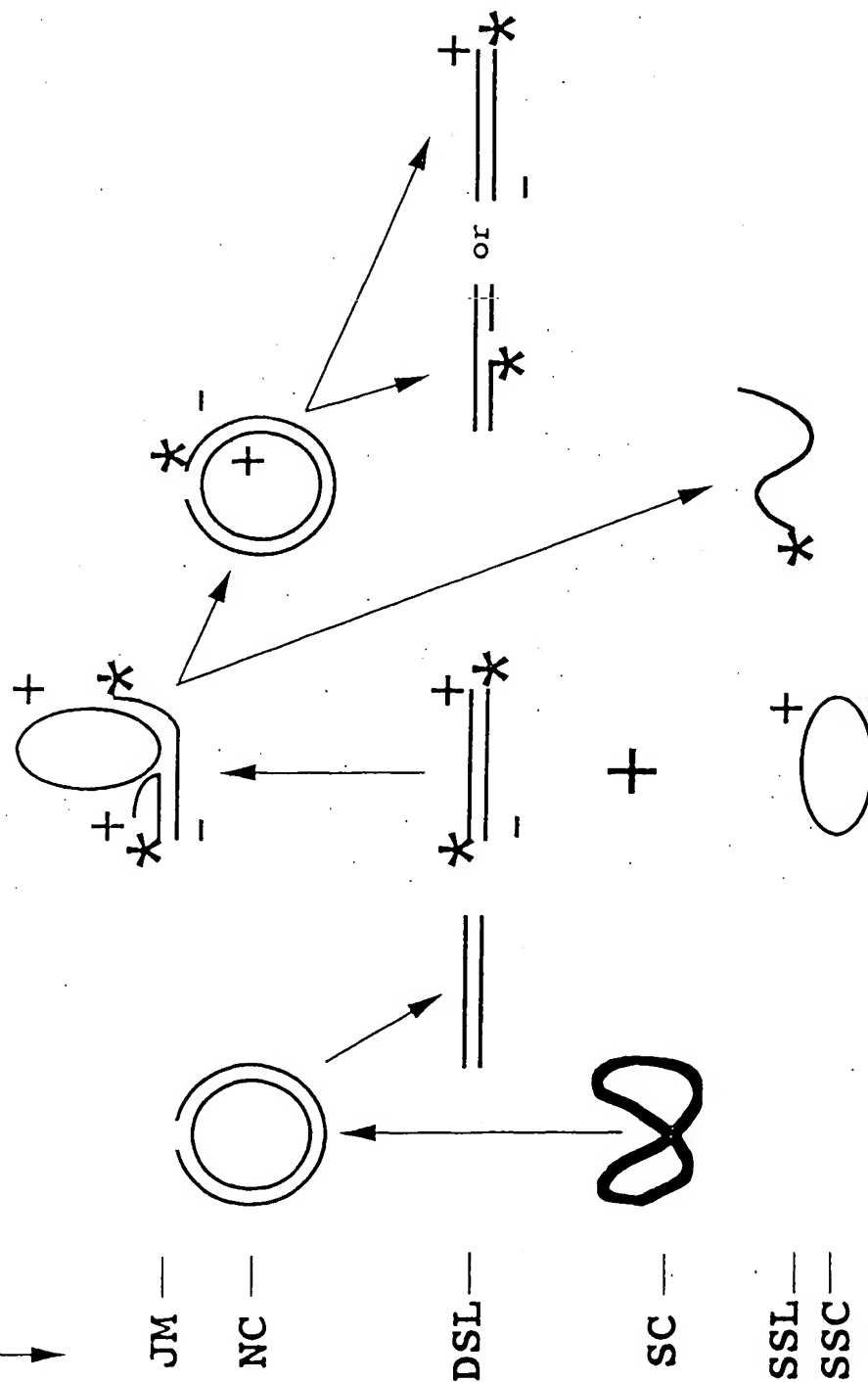


FIG. 8



Electrophoretic Migration

FIG. 9



Topoisomerase DNA Cleavage JM, NC & SSL Form
Typical Strand Transfer Plus Topoisomerase Activity DS Lin. & SS Lin. Form

DRAP

RecA + SSB

DRAP

FIG. 10

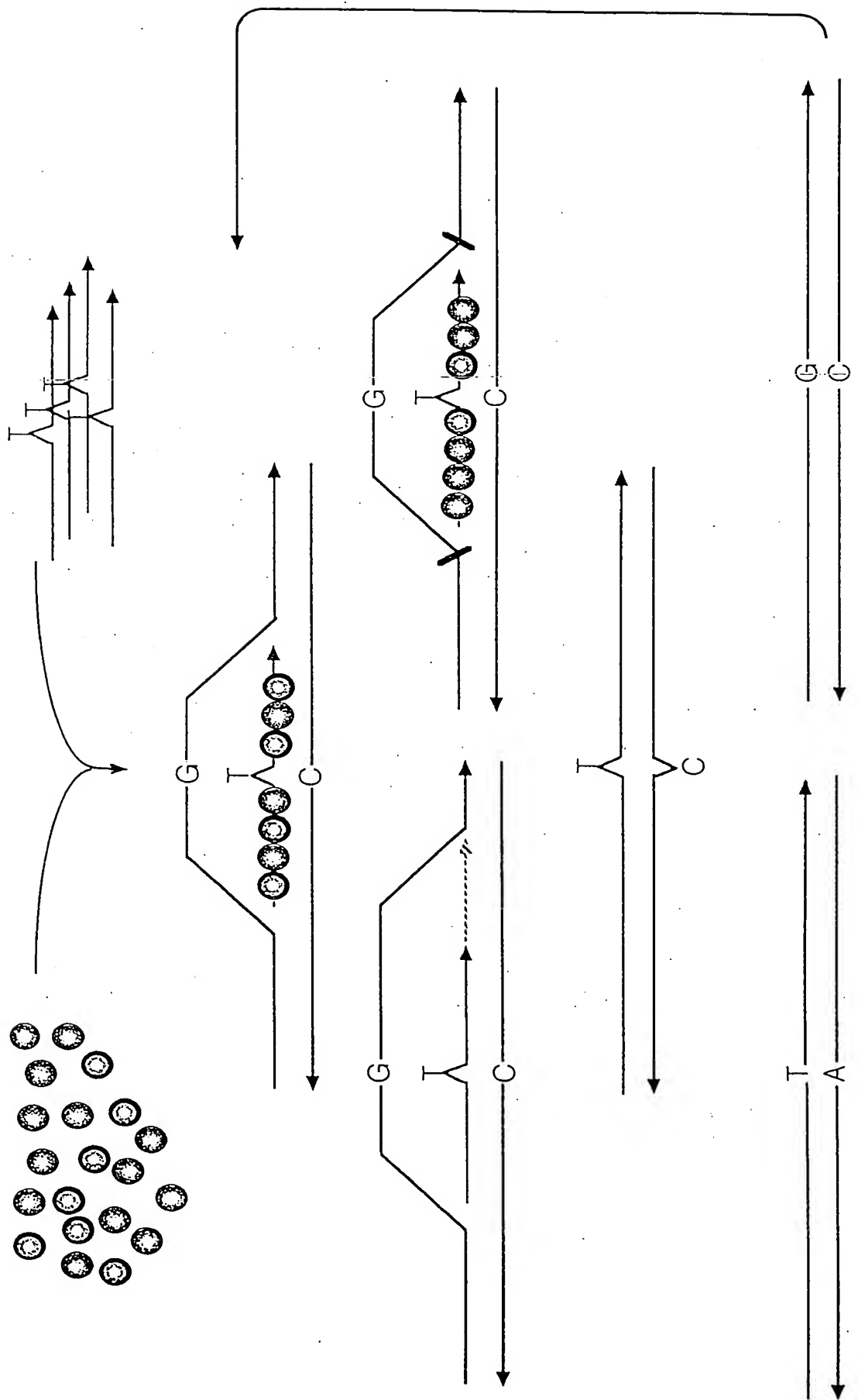


FIG. 12A

Murine c-Kit Exon 17

18 bp RFPL

|<----->|

Intron:

gga cag

=====

DpnI

Sau3AI

EciI

AciI

BscGI

MnlI

MnlI

AlwI

BseRI

ScrFI

CviJI

ECORI

Fnu4HI

TseI

BbvI

SthI32I

CDNA: tgtattcacagagatttgccagccaggaaatcctcctcactcagggcggtacacaaag
2384

acataagtggtctctctaaaccgtcggtccttataggaggagtgagtgccgccttagtttc

C I H R D L A A R N I L L T H G R I T K -

CviJI

BsmAI

Cac8I

BfaI

CviJI

NheI

|||

Tsp509I

NspV

TaqI

HinfI

TfiI

|||

BsaAI

MaeII

|||

SthI32I

atttgcgatttcgggctagccagagacatcaggaatgattcggaattacgtgggtcaaaaggaaatg
2444
taaacgctaagcccgatcggtctctgtagtccttactaagcttaatgcaccagtttcctttac

I C D F G L A R D I R N D S N Y V V K G N

A-----A

FIG. 12B

A-----A

W42 Mutation

	BseRI		DpnI
	SacRI		Sau3AI
	CviJI		EciI
	EcoRII		AciI
	Fnu4HI		BscGI
	TseI	Sth132I	MnlI
		BbvI	MnlI
			AlwI

1 tgtaattcacagaaatttggcagccaggaaataatcctcactcagggcgatcacaag + 60
 acataagtgtctttaaacggtcggtccttataggaggagtgagtgcccgccagtgtttc

C I H R N L A A R N I L L T H G R I T K -

Mutation & RFLP

Underline: Potential Mutagenic Oligo
 =====> <===== Potential PCR Primers for RFLP Analysis

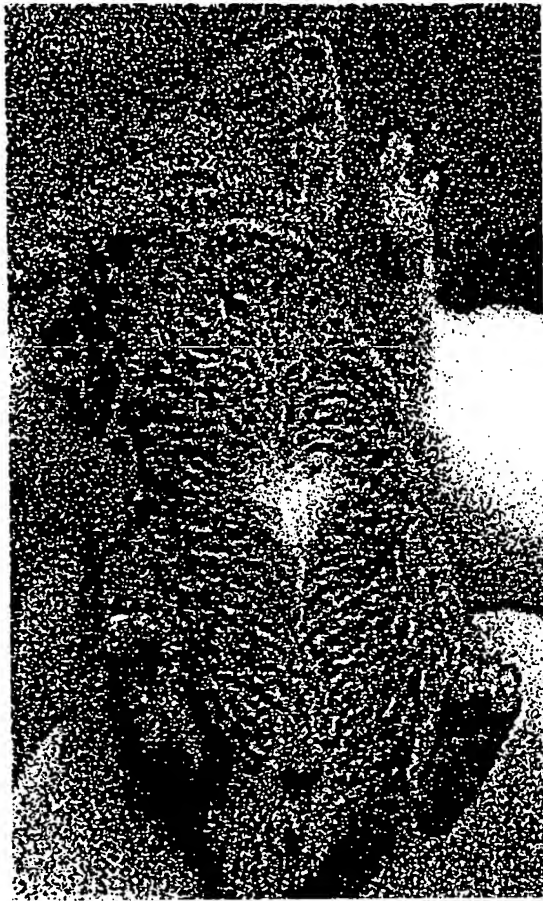


FIG. 13A



FIG. 13B